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<120> Regulation of Human Transient Receptor Potential Channel

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<150> US 60/372,899
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His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
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Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
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Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
Page 22

Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
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His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val
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Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
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His Thr His Leu Leu Leu Val Asp Asn Gly Cys His Gly His Pro Thr
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Ala Met Phe Gly Tyr Thr Val Gly Thr Val Gln Glu Asn Asn Asp Gln
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980

985

990

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Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
Page 31

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170

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Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn
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Glu Lys His Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly
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Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val
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Glu Gly Ser Gly Arg Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val
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Glu Asp Ala Pro Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe
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Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
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Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
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 Gln His Phe Thr Ala Gln Pro Gly Val Gln Asn Phe Leu Ser Lys Gln
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 Trp Tyr Gly Glu Ile Ser Arg Asp Thr Lys Asn Trp Lys Ile Ile Leu
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 Cys Leu Phe Ile Ile Pro Leu Val Gly Cys Gly Phe Val Ser Phe Arg
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 Lys Lys Pro Val Asp Lys His Lys Lys Leu Leu Trp Tyr Tyr Val Ala
 705 710 715 720

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Val Gln Glu Tyr Cys Ser Arg Leu Asn Ile Pro Phe Pro Phe Ile Val
995 1000 1005

Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys
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Cys Lys Glu Lys Asn Met Glu Ser Ser Val Cys Cys Phe Lys Asn
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Tyr Leu Val Lys Ile Asn Thr Lys Ala Asn Asp Thr Ser Glu Glu
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Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
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Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
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His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
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Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile
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Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn
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355 360 365

Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
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Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
Page 36

385

390

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Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
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Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
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Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
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Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
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Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile
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Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys
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Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala
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Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
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Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp
Page 39

85

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Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
100 105 110

Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
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His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
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Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile
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Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val
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Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp
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Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
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 Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
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 Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
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 Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
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Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
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His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
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Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile
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Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
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Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
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 Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn
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 Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu
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 Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly
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 Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu
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 Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val
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 Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val
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 Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe
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 Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp
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 Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
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 Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
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 Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
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 Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
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 Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
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 Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
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His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val
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Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
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Cys Leu Phe Ile Ile Pro Leu Val Gly Cys Gly Phe Val Ser Phe Arg
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Lys Lys Pro Val Asp Lys His Lys Lys Leu Leu Trp Tyr Tyr Val Ala
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Phe Phe Thr Ser Pro Phe Val Val Phe Ser Trp Asn Val Val Phe Tyr
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Ile Ala Phe Leu Leu Leu Phe Ala Tyr Val Leu Leu Met Asp Phe His
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Ser Val Pro His Pro Pro Glu Leu Val Leu Tyr Ser Leu Val Phe Val
Page 44

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Thr	Thr	Tyr	Asp	Phe	Ala	His	Cys	Thr	Phe	Thr	Gly	Asn	Glu	Ser	Lys
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Phe	Ala	Tyr	Phe	Tyr	Met	Val	Val	Lys	Lys	Cys	Phe	Lys	Cys	Cys	
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Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
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His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
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Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
Page 47

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Phe Lys Lys Arg Glu Cys Val Phe Phe Thr Lys Asp Ser Lys Ala Thr
50 55 60
Glu Asn Val Cys Lys Cys Gly Tyr Ala Gln Ser Gln His Met Glu Gly
65 70 75 80
Thr Gln Ile Asn Gln Ser Glu Lys Trp Asn Tyr Lys Lys His Thr Lys
85 90 95
Glu Phe Pro Thr Asp Ala Phe Gly Asp Ile Gln Phe Glu Thr Leu Gly
100 105 110
Lys Lys Gly Lys Tyr Ile Arg Leu Ser Cys Asp Thr Asp Ala Glu Ile
115 120 125
Leu Tyr Glu Leu Leu Thr Gln His Trp His Leu Lys Thr Pro Asn Leu
130 135 140
Val Ile Ser Val Thr Gly Gly Ala Lys Asn Phe Ala Leu Lys Pro Arg
145 150 155 160
Met Arg Lys Ile Phe Ser Arg Leu Ile Tyr Ile Ala Gln Ser Lys Gly
165 170 175
Ala Trp Ile Leu Thr Gly Gly Thr His Tyr Gly Leu Met Lys Tyr Ile
180 185 190
Gly Glu Val Val Arg Asp Asn Thr Ile Ser Arg Ser Ser Glu Glu Asn
195 200 205
Ile Val Ala Ile Gly Ile Ala Ala Trp Gly Met Val Ser Asn Arg Asp
210 215 220
Thr Leu Ile Arg Asn Cys Asp Ala Glu Gly Tyr Phe Leu Ala Gln Tyr
225 230 235 240
Leu Met Asp Asp Phe Thr Arg Asp Pro Leu Cys Ile Leu Asp Asn Asn
245 250 255
His Thr His Leu Leu Leu Val Asp Asn Gly Cys His Gly His Pro Thr
260 265 270
Val Glu Ala Lys Leu Arg Asn Gln Leu Glu Lys Tyr Ile Ser Glu Arg
275 280 285
Thr Ile Gln Asp Ser Asn Tyr Gly Gly Lys Ile Pro Ile Val Cys Phe
290 295 300
Ala Gln Gly Gly Gly Lys Glu Thr Leu Lys Ala Ile Asn Thr Ser Ile
305 310 315 320

Lys Asn Lys Ile Pro Cys Val Val Val Glu Gly Ser Gly Gln Ile Ala
325 330 335

Asp Val Ile Ala Ser Leu Val Glu Val Glu Asp Ala Leu Thr Ser Ser
340 345 350

Ala Val Lys Glu Lys Leu Val Arg Phe Leu Pro Arg Thr Val Ser Arg
355 360 365

Leu Pro Glu Glu Glu Thr Glu Ser Trp Ile Lys Trp Leu Lys Glu Ile
370 375 380

Leu Glu Cys Ser His Leu Leu Thr Val Ile Lys Met Glu Glu Ala Gly
385 390 395 400

Asp Glu Ile Val Ser Asn Ala Ile Ser Tyr Ala Leu Tyr Lys Ala Phe
405 410 415

Ser Thr Ser Glu Gln Asp Lys Asp Asn Trp Asn Gly Gln Leu Lys Leu
420 425 430

Leu Leu Glu Trp Asn Gln Leu Asp Leu Ala Asn Asp Glu Ile Phe Thr
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Asn Asp Arg Arg Trp Glu Ser Ala Asp Leu Gln Glu Val Met Phe Thr
450 455 460

Ala Leu Ile Lys Asp Arg Pro Lys Phe Val Arg Leu Phe Leu Glu Asn
465 470 475 480

Gly Leu Asn Leu Arg Lys Phe Leu Thr His Asp Val Leu Thr Glu Leu
485 490 495

Phe Ser Asn His Phe Ser Thr Leu Val Tyr Arg Asn Leu Gln Ile Ala
500 505 510

Lys Asn Ser Tyr Asn Asp Ala Leu Leu Thr Phe Val Trp Lys Leu Val
515 520 525

Ala Asn Phe Arg Arg Gly Phe Arg Lys Glu Asp Arg Asn Gly Arg Asp
530 535 540

Glu Met Asp Ile Glu Leu His Asp Val Ser Pro Ile Thr Arg His Pro
545 550 555 560

Leu Gln Ala Leu Phe Ile Trp Ala Ile Leu Gln Asn Lys Lys Glu Leu
565 570 575

Ser Lys Val Ile Trp Glu Gln Thr Arg Gly Cys Thr Leu Ala Ala Leu
580 585 590

Gly Ala Ser Lys Leu Leu Lys Thr Leu Ala Lys Val Lys Asn Asp Ile
Page 50

595					600					605					
Asn	Ala	Ala	Gly	Glu	Ser	Glu	Glu	Leu	Ala	Asn	Glu	Tyr	Glu	Thr	Arg
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Ala	Val	Glu	Leu	Phe	Thr	Glu	Cys	Tyr	Ser	Ser	Asp	Glu	Asp	Leu	Ala
625					630					635					640
Glu	Gln	Leu	Leu	Val	Tyr	Ser	Cys	Glu	Ala	Trp	Gly	Gly	Ser	Asn	Cys
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Leu	Glu	Leu	Ala	Val	Glu	Ala	Thr	Asp	Gln	His	Phe	Ile	Ala	Gln	Pro
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Gly	Val	Gln	Asn	Phe	Leu	Ser	Lys	Gln	Trp	Tyr	Gly	Glu	Ile	Ser	Arg
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Lys	Lys	Leu	Leu	Trp	Tyr	Tyr	Val	Ala	Phe	Phe	Thr	Ser	Pro	Phe	Val
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Val	Phe	Ser	Trp	Asn	Val	Val	Phe	Tyr	Ile	Ala	Phe	Leu	Leu	Leu	Phe
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Ala	Tyr	Val	Leu	Leu	Met	Asp	Phe	His	Ser	Val	Pro	His	Pro	Pro	Glu
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Leu	Val	Leu	Tyr	Ser	Leu	Val	Phe	Val	Leu	Phe	Cys	Asp	Glu	Val	Arg
	770					775					780				
Gln	Trp	Tyr	Val	Asn	Gly	Val	Asn	Tyr	Phe	Thr	Asp	Leu	Trp	Asn	Val
785					790					795					800
Met	Asp	Thr	Leu	Gly	Leu	Phe	Tyr	Phe	Ile	Ala	Gly	Ile	Val	Phe	Arg
				805					810					815	
Leu	His	Ser	Ser	Asn	Lys	Ser	Ser	Leu	Tyr	Ser	Gly	Arg	Val	Ile	Phe
			820					825					830		
Cys	Leu	Asp	Tyr	Ile	Ile	Phe	Thr	Leu	Arg	Leu	Ile	His	Ile	Phe	Thr
		835					840					845			
Val	Ser	Arg	Asn	Leu	Gly	Pro	Lys	Ile	Ile	Met	Leu	Gln	Arg	Met	Leu
	850					855					860				
Ile	Asp	Val	Phe	Phe	Phe	Leu	Phe	Leu	Phe	Ala	Val	Trp	Met	Val	Ala
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Phe Gly Val Ala Arg Gln Gly Ile Leu Arg Gln Asn Glu Gln Arg Trp
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Arg Trp Ile Phe Arg Ser Val Ile Tyr Glu Pro Tyr Leu Ala Met Phe
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Gly Gln Val Pro Ser Asp Val Asp Gly Thr Thr Tyr Asp Phe Ala His
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Cys Thr Phe Thr Gly Asn Glu Ser Lys Pro Leu Cys Val Glu Leu Asp
930 935 940

Glu His Asn Leu Pro Arg Phe Pro Glu Trp Ile Thr Ile Pro Leu Val
945 950 955 960

Cys Ile Tyr Met Leu Ser Thr Asn Ile Leu Leu Val Asn Leu Leu Val
965 970 975

Ala Met Phe Gly Tyr Thr Val Gly Thr Val Gln Glu Asn Asn Asp Gln
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Val Trp Lys Phe Gln Arg Tyr Phe Leu Val Gln Glu Tyr Cys Ser Arg
995 1000 1005

Leu Asn Ile Pro Phe Pro Phe Ile Val Phe Ala Tyr Phe Tyr Met
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Val Val Lys Lys Cys Phe Lys Cys Cys Cys Lys Glu Lys Asn Met
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Ala Trp Glu Gly Val Met Lys Glu Asn Tyr Leu Val Lys Ile Asn
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Thr Lys Ala Asn Asp Thr Ser Glu Glu Met Arg His Arg Phe Arg
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Ile Ala Asn Lys Ile Lys
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Arg Asn Asp Thr Leu Asp Ser Thr Arg Thr Leu Tyr Ser Ser Ala Ser
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Arg Ser Thr Asp Leu Ser Tyr Ser Glu Ser Ala Ser Phe Tyr Ala Ala
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Phe Arg Thr Gln Thr Cys Pro Ile Met Ala Ser Trp Asp Leu Val Asn
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Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe Thr Lys
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Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala Gln Ser
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Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp Asn Tyr
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Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp Ile Gln
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Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser Cys Asp
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Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp His Leu
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Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys Asn Phe
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Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile Tyr Ile
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Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His Tyr Gly
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Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile Ser Arg
225 230 235 240

Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp Gly Met
245 250 255

Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu Gly Tyr
260 265 270

Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro Leu Tyr
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275

280

285

Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn Gly Cys
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His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu Glu Lys
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Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly Lys Ile
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Pro Ile Val Cys Phe Ala Gln Gly Gly Lys Glu Thr Leu Lys Ala
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Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val Glu Gly
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Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val Glu Asp
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Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe Leu Pro
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Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp Ile Lys
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Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val Ile Lys
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Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser Tyr Ala
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Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn Trp Asn
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Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu Ala Asn
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Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Lys Ser Lys Pro Arg
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Leu Arg Asp Thr Ile Ile Gln Val Thr Trp Leu Glu Asn Gly Arg Ile
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Lys Val Glu Ser Lys Asp Val Thr Asp Gly Lys Ala Ser Ser His Met
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Leu Val Val Leu Lys Ser Ala Asp Leu Gln Glu Val Met Phe Thr Ala
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 Ser Asn His Phe Ser Thr Leu Val Tyr Arg Asn Leu Gln Ile Ala Lys
 580 585 590
 Asn Ser Tyr Asn Asp Ala Leu Leu Thr Phe Val Trp Lys Leu Val Ala
 595 600 605
 Asn Phe Arg Arg Gly Phe Arg Lys Glu Asp Arg Asn Gly Arg Asp Glu
 610 615 620
 Met Asp Ile Glu Leu His Asp Val Ser Pro Ile Thr Arg His Pro Leu
 625 630 635 640
 Gln Ala Leu Phe Ile Trp Ala Ile Leu Gln Asn Lys Lys Glu Leu Ser
 645 650 655
 Lys Val Ile Trp Glu Gln Thr Arg Gly Cys Thr Leu Ala Ala Leu Gly
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 675 680 685
 Ala Ala Gly Glu Ser Glu Glu Leu Ala Asn Glu Tyr Glu Thr Arg Ala
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 Val Gly Glu Ser Thr Val Trp Asn Ala Val Val Gly Ala Asp Leu Pro
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 Cys Gly Thr Asp Ile Ala Ser Gly Thr His Arg Pro Asp Gly Gly Glu
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 Leu Phe Thr Glu Cys Tyr Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu
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 Ala Val Glu Ala Thr Asp Gln His Phe Ile Ala Gln Pro Gly Val Gln
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 Asn Phe Leu Ser Lys Gln Trp Tyr Gly Glu Ile Ser Arg Asp Thr Lys
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 Asn Trp Lys Ile Ile Leu Cys Leu Phe Ile Ile Pro Leu Val Gly Cys
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 Gly Phe Val Ser Phe Arg Lys Lys Pro Val Asp Lys His Lys Lys Leu
 820 825 830

Leu Trp Tyr Tyr Val Ala Phe Phe Thr Ser Pro Phe Val Val Phe Ser
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Trp Asn Val Val Phe Tyr Ile Ala Phe Leu Leu Leu Phe Ala Tyr Val
850 855 860

Leu Leu Met Asp Phe His Ser Val Pro His Pro Pro Glu Leu Val Leu
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Tyr Ser Leu Val Phe Val Leu Phe Cys Asp Glu Lys Arg Lys Thr Ala
885 890 895

Met Asp Gln Thr Asp Glu Asp Leu Phe Pro Tyr Gly Ala Phe Tyr Gln
900 905 910

Phe Leu Met Ile Ser Arg Ser Phe Arg Gly Glu Glu Met Ser Ile Gly
915 920 925

Lys Gln His
930